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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,916	07/09/2001	Hiroshi Shiku	P20854	1184

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,916	SHIKU ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-26 are being acted upon.

2. Applicant's amendment, remarks, and duplicate IDS, filed 12/12/05, are acknowledged. In view of Applicant's amendment, the previous rejection under the first paragraph of 35 U.S.C. 112 has been withdrawn.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States

4. Claims 1-3, 6, 11, 12, 15, 18, and 20 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Kohno et al. 1996.

As set forth previously, Kohno et al. teaches a DC APC capable of inducing cellular immunity, said cell having been produced by reacting *in vitro* with the hydrophobized polysaccharide pullulan (see particularly page 213, column 1).

Note that Claim 1 now recites a cell capable of inducing cytotoxic T cells (CTLs). The reference teaches the use of spleen-derived APCs (page 212, column 2). Said cells would include dendritic cells (DCs). It is well-established in the immunological arts that DCs are the most effective of the APCs and are indeed capable of inducing CTLs.

Applicant's arguments, filed 12/12/05, have been fully considered but they are not persuasive. Applicant argues that the protein of Kohno could be both an antigen and a hydrophobizing agent, while the instant claims and specification are directed to a complex, i.e., a conjugate.

Applicant is advised that the reference teaches the use of an SBP-pullulan conjugate.

Applicant argues that the T cells of the reference are CD4+ cells and not CTLs.

Applicant is advised that the claims are not drawn to CTLs, but rather cells capable of inducing CTLs. The SBP-pullulan-loaded APCs of the claims meet this limitation.

Applicant argues, "Further, Sugi-basic protein disclosed in Kohno is an extracellularly-derived antigen and not an antigen produced by a pathologic virus and the like which is infective to human cells. Therefore, it appears that a cell activated by using Sugi-basic protein will not induce cytotoxic T cell (CTL)".

Applicant is advised that the point of this argument cannot be determined. SBP comprises an antigen no different from any other, indeed, it is actually established in the reference that SBP is capable of inducing an immune response given that it is a known allergen.

Applicant argues that the purpose of the research taught by the reference is different that the purpose of the instant invention.

Applicant is advised that said difference is irrelevant. The reference teaches a product and method comprising the limitations of the product and method of the instant claims.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-24 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Nestle et al. (1998, IDS) in view of Gu et al. (1997, IDS).

As set forth previously, Nestle et al. teaches a method for inducing cellular immunity comprising isolating a DC APC, reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration (see particularly Methods, page 331, column 2 - page 332, column 1).

The reference differs from the claimed invention only in that it does not teach an APC loaded with the ErbB-2 antigen by reacting with a complex comprising a

hydrophobized polysaccharide comprising mannan or a polysaccharide comprising the limitations of Claim 4 wherein the sterol is cholesterol.

Gu et al. teaches that a cholesterol bearing mannan polysaccharide complexed to an ErbB-2 antigen (an antigen overexpressed in a wide range of human adenocarcinomas, see Abstract) can be used to induce CD8+ CTLs (page 19, column 2, second full paragraph and page 23, column 1) by a mechanism of facilitating the entry of the antigen into the MHC Class I pathway for presentation by APCs (see particularly page 24, column 1, first full paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a product for, and perform a method for, inducing cellular immunity comprising isolating a DC APC, reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration, as taught by Nestle et al. One of ordinary skill in the art at the time of the invention would have been motivated to employ the cholesterol bearing mannan polysaccharide complexed to an ErbB-2 antigen of Gu et al. given the teachings of the reference that the ErbB-2 antigen is overexpressed in a wide range of human adenocarcinomas (and would thus provide an obvious target for immunotherapy) and that the use of the cholesterol bearing mannan polysaccharide facilitates the entry of the antigen into the MHC Class I pathway for presentation by APCs.

Applicant's arguments, filed 12/12/05, have been fully considered but they are not persuasive. Applicant summarizes the teachings of the references and concludes that the combined references target a different intended APC pathway and a different intended mechanism.

Applicant is advised that the combined references need only meet the claimed limitations. Intended pathways and mechanisms have no bearing on patentability.

Applicant argues that the "Appellant's invention does not establish unexpected results".

Said lack of unexpected results is noted.

Regarding unexpected results, Applicants note that the Office Action is apparently requiring that Applicants compare their invention to their own invention.

Applicant is advised that no such requirement has been set forth.

Applicant asserts advantages and unexpected results of the instantly claimed subject matter over the combined teachings of the prior art.

Applicant is advised that asserted "advantages" do not render the invention of the instant claims patentably distinct

from the invention of the prior art. It is unclear why Applicant would state "Appellant's invention does not establish unexpected results" at page 16 of the instant Remarks, yet at page 18 assert "... unexpected results associated with Applicants' invention over the prior art utilized in the rejections ..."? This sort of inconsistent argument is difficult to address.

Applicant is advised that it is well-established that it is inappropriate to assert superior or unexpected results not disclosed in the specification in an attempt to overcome an art rejection. Additionally, it is unclear how or why Applicant can or would compare Figure 1 of Wang et al. *Int. J. Oncol.* (1999), which discloses *in vivo* tumor size after DC vaccination as a function of time, with Figure 5 of Gu et al., which discloses *in vitro* spleen cell killing activity, with Figure 5 of Wang et al., which discloses another example of *in vivo* tumor size after DC vaccination as a function of time.

Applicant argues that the polysaccharide of the prior art cannot form a complex with a tumor antigen.

Applicant is advised that the prior art teaches a complex of a cholesterol bearing mannan polysaccharide and a HER2 antigen (page 20, column 2).

As set forth previously, the Examiner's burden is merely to establish motivation to produce the claimed invention. Said motivation need not be Applicant's. Said motivation has been properly established as set forth above.

7. Claims 1-26 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Nestle et al. (1998, IDS) in view of Gu et al. (1998, of record).

As set forth previously, Nestle et al. has been discussed above.

The reference differs from the claimed invention only in that it does not teach an APC loaded with antigen (ErbB2 also known as HER2) by reacting with a complex comprising a hydrophobized polysaccharide comprising mannan or pullulan, or a polysaccharide comprising the limitations of Claim 4 wherein the sterol is cholesterol.

Gu et al. teaches that a cholesterol bearing mannan or pullulan polysaccharide complexed to a HER2 antigen (see Materials and Methods) can be used to induce CD8+ cellular immunity (see particularly Figures 1 and 4), while antigen alone is ineffective, by a mechanism of facilitating the entry of the antigen into an APC through a carbohydrate-recognizing receptor such as DEC-205, and entry into the

cytosol (for transport to MHC Class I) after phagocytosis (see particularly page 3389, column 2-3390).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a product for, and perform a method for, inducing cellular immunity comprising isolating a DC APC, reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration, as taught by Nestle et al. One of ordinary skill in the art at the time of the invention would have been motivated to employ the cholesterol bearing mannan or pullulan polysaccharide complexed to a HER2 antigen of Gu et al. given the teachings of the reference that hydrophobized polysaccharide-antigen complex facilitates the entry of the antigen into an APC through a carbohydrate-recognizing receptor such as DEC-205, and entry into the cytosol (for transport to MHC Class I) after phagocytosis, for superior antigen presentation and cellular immunity.

This rejection has not been traversed separately.

8. The following is a new ground of rejection necessitated by Applicant's amendment.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-26 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) a cell capable of inducing cytotoxic T cells, said cell comprising an *in vitro* reaction product of a complex with an antigen-presenting cell, said complex formed from mixing of a hydrophobized polysaccharide and an antigen inducing cytotoxic T cells. (Claim 1).

B) a method for preparing a cell capable of inducing cellular immunity, comprising reacting *in vitro* a complex with an antigen-presenting cell, said complex formed from mixing of a hydrophobized polysaccharide and an antigen inducing cytotoxic T cells. (Claim 11).

Applicant indicates that support for the new limitations can be found at pages 1, 4, 6, and 7 of the specification.

Regarding A, while the term CTL is found at pages 1, 4, and 6, there is no disclosure of a generic cell capable of inducing a CTL.

Regarding B, the "mixing" at page 7 is of a "hydrophobized polysaccharide and antigen" as a method for encapsulating antigens. There is no disclosure of a generic mixing of "hydrophobized polysaccharide and an antigen inducing cytotoxic T cells" as claimed.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically:

A) the grammatically-improper phrase "an antigen inducing cytotoxic T cells" cannot be interpreted in the context of Claims 1, 1, 13, and 20.

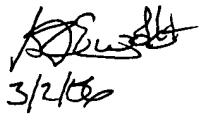
13. No claim is allowed.

14. Applicant has again submitted an IDS listing numerous foreign documents for which no certified translations have been provided. Applicant is advised that absent certified translations, concise explanations of the relevance of the information presented in the documents to the claimed invention is required. See MPEP 609.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

17. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.



3/2/06

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